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Feasibility of Assessment of Health Risks from Vapor-Phase Organic Chemicals in Gasoline and Diesel Exhaust

National Research Council, Washington, DC

Prepared for

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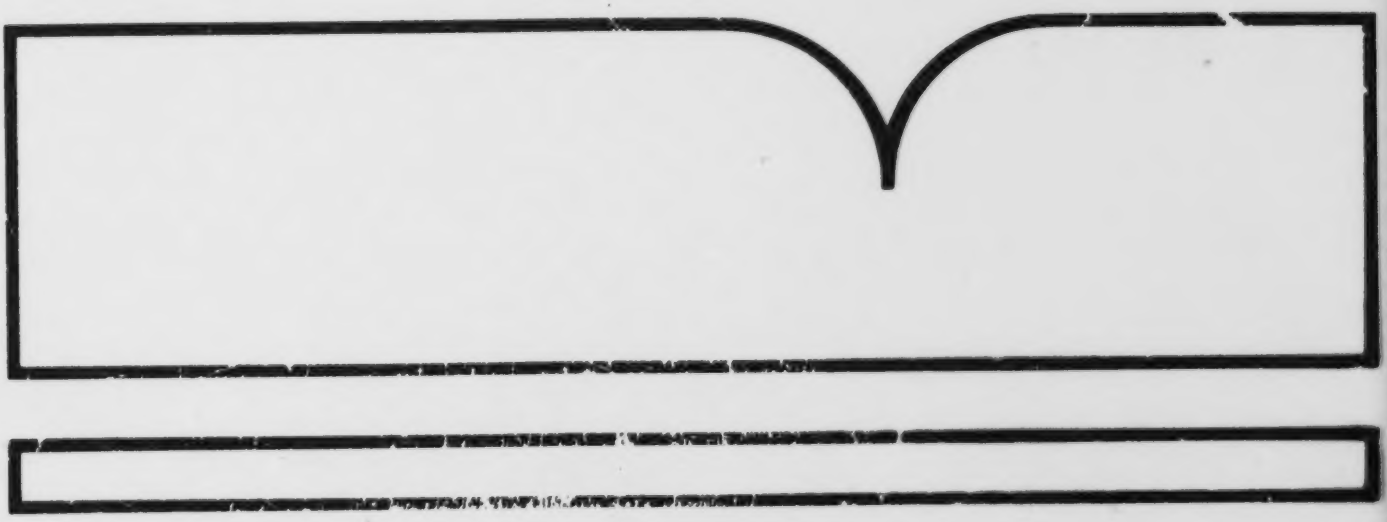

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FEASIBILITY OF ASSESSMENT OF HEALTH RISKS FROM VAPOR-PHASE ORGANIC CHEMICALS IN GASOLINE AND DIESEL EXHAUST

Prepared by the

Committee on Vapor-Phase Organics

Board on Toxicology and Environmental Health Hazards

Commission on Life Sciences

National Research Council

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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The Committee was asked to develop a list of organic chemicals identified in the vapor phase in exhaust from diesel- and gasoline-fueled engines and to explore the availability of toxicologic and epidemiologic information on each of them for use in making a quantitative and qualitative assessment of the human health risk associated with exposure to such exhaust.

The committee determined that quantitative risk assessment could probably be applied to only three to five vapor-phase components of diesel exhaust: formaldehyde, benz[a]-anthracene, acrolein, and perhaps 2-nitroflourene and chrysene. Data on the others seem insufficient for detailed quantitative risk assessment, although comparative risk assessment or qualitative risk assessment would be possible.

Readers may find interesting the listings in the appendix of specific chemicals in exhaust of engines as summarized from published literature.

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INTRODUCTION

This report describes the findings of what was tentatively planned as the first part of a two-part study conducted by the Committee on Vapor-Phase Organics in the Board on Toxicology and Environmental Health Hazards of the National Research Council's Commission on Life Sciences. This part of the study is referred to hereafter as the feasibility study. It was supported by a contract between the National Academy of Sciences and the Enviromental Protection Agency (EPA). The Committee was asked to develop a list of organic chemicals identified in the vapor phase* in exhaust from diesel- and gasoline-fueled engines and to explore the availability of toxicologic and epidemiologic information on each of them for use in making a quantitative and qualitative assessment of the human health risk associated with exposure to such exhaust. If sufficient toxicologic and epidemiologic information were available on five to 10 representative vapor-phase organic chemicals, the Committee was asked to conduct the second part of the study, wherein it would assess the human health risks associated with these chemicals as emitted in exhaust from diesel or gasoline engines or both.

Readers of this report should be aware of how the information presented was intended to be used. Some citations to the published literature on the candidate chemicals were not in the data files searched and thus were not used. In its "Strategy for Selecting the Chemicals Used in This Study," the Committee explained "it should be emphasized that the Committee's efforts were directed toward determining the feasibility of performing a risk assessment for chemicals present in vehicle exhaust and that the Committee operated under severe time constraints. There was no exhaustive attempt to review all the published literature; what was asked was whether sufficient information existed on human health and magnitudes of exposure to each of these chemicals that might be used in risk assessment."

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*Organic chemicals in the vapor phase that are not collected on a glass-fiber filter in a dilution tunnel at less than 125°F, as described in the federal testing procedure.

BACKGROUND OF THE STUDY

Federal, state, and private agencies have made substantial efforts to assess the adverse effects on human health of exposure to exhaust from all types of vehicles burning all types of fuels. In 1974, the oil embargo brought attention to the need to conserve energy and led to an emphasis on improving efficiency of fuel use in vehicles. Later, the percentage of more fuel-efficient diesel-engine vehicles in the light-duty fleet increased.

In 1977, with the greater use of the fuel-efficient diesel vehicles, researchers focused on the heavy emission of soot from diesel engines--particularly important because of the potential impact of this emission on the ability to meet national ambient-air standard for particles. It became a matter of broad national concern whether an increase in the number of diesel vehicles in use would contribute substantially to an increase in atmospheric particles in areas of heavy traffic. Research therefore was aimed mostly at measuring particulate emission and then at measuring the chemicals adsorbed on the particles. The focus on the potential impact of diesel-exhaust particles on the health of exposed humans led to a narrowing of the attention given to the emitted vapor-phase substances that were not bound to particulate matter or trapped by the particle-collecting filters described in federal testing procedures.

In its 1982 Research Outlook, a report to Congress, the EPA stated that previous efforts to control emission from mobile sources had been a key element in the overall national program to protect the public from the adverse effects of air pollution (U. S. EPA, 1982). One of EPA's specific concerns was the emission of 30-100 times more particles by diesel-powered, light-duty vehicles than by gasoline-powered vehicles. The complex problem, as stated, has been to identify the biologically active elements in diesel exhaust, estimate the likely extent of human exposure to them, and assess the human cancer risk posed by increased use of diesel engines. The EPA report stated that experts had concluded that even a major increase in the diesel fleet would not pose a threat to public health. However, its research strategy included the need for refined exposure assessment and measurement techniques so that it could more accurately evaluate the effects of gaseous and particulate emission from

diesel engines on human health and welfare. It needed procedures for detecting and characterizing the activity and potency of chemical mutagens and other hazardous pollutants and for investigating their relationships in the particulate and gaseous phases in tailpipe emission from both diesel and gasoline engines (including real-time analysis of such substances as the so-called priority unregulated pollutants, e.g., formaldehyde).

In 1981, Harris assessed the risk of human lung cancer associated with exposure to diesel-engine emission. The procedure was based on the critical assumption that relative carcinogenic potencies of diesel emission "are preserved across human and nonhuman biological systems." This assumption needs to be regarded as at best an approximation, in view of the interspecies and interorgan differences in particle distribution, extractability and clearance of particle-bound chemicals, target site of action, metabolism, and genetic repair mechanisms. On the basis of the incidence of lung cancer in diesel-bus garage workers of the London Transport Authority, Harris determined the upper confidence limit of potential risk, by two methods of analysis, to be a 0.05% or 0.03% increase in lung-cancer incidence per unit of exposure to diesel emission; 1 unit of exposure is equivalent to inhaling particles at 1 $\mu g/m^3$ of air for 1 yr. Harris assumed that cumulative lifetime exposure to diesel emission was linear.

In 1981, an NRC committee (NRC, 1981) conducted a detailed and comprehensive study of health effects associated with exposure to diesel exhaust. The panel concluded that "evidence of genotoxic activity and hence possible carcinogenic activity is clearly demonstrated in the results obtained with short-term in vitro studies." However, it also stated that whole diesel- or gasoline-engine exhaust had not been found to be carcinogenic when inhaled by laboratory animals, although large-scale studies were under way when the report was being prepared. Skin carcinogenesis had been found to occur in studies with both diesel- and gasoline-engine exhaust extracts. The report stated that "mouse skin carcinogenicity data and other quantitative bioassay data can be used to estimate the relative carcinogenicity of organic extracts of both diesel exhaust and related environmental emissions." The report noted that data on pulmonary and systemic effects had confirmed that the "fibrogenic potential of diesel exhaust is low," that pulmonary defense mechanisms may be adversely affected (it was unclear whether this phenomenon is associated with the gaseous or particulate phase of the exhaust), and that it is possible to estimate the health hazards associated with the expected increase in gaseous and particulate components contributed by diesel engines in the general atmosphere. The findings from epidemiologic studies have not convincingly demonstrated an excess of lung cancer in persons occupationally exposed to diesel-engine emission. It was concluded that the available evidence did not indicate that exposure to diesel exhaust is a serious cancer hazard--at least in the case of exposures no greater than those in the London Transport Authority bus garage studies. However, the NRC report also stated that "essentially no information is available concerning the carcinogenicity of gas-phase components."

STRATEGY FOR SELECTING THE CHEMICALS USED IN THIS STUDY

The charge to this Committee was to determine the feasibility of assessing human health risk associated with the emission of vapor-phase organic substances from diesel- or gasoline-powered automotive engines and comparing the risk by fuel type, and to explore whether information was sufficient on five to 10 representative chemicals to permit quantitative risk analysis. (The upper bound of 10 compounds was based on an idea of the amount of information that could be collected and reviewed by the Committee in the short time allowed for this feasibility study. The lower bound of five was chosen because it was assumed that at least that number would be required for performance of a reasonably representative quantitative risk assessment.)

Considering the importance of this subject and the extent of research undertaken by government and industry over the last 10 yr, the Committee expected to find a comprehensive tabulation of the chemicals emitted in exhaust from all types of engines. Only by systematic examination of a listing of the chemicals emitted could those known to be hazardous or suspected of being hazardous to human health be identified. The Committee requested such a list from EPA and was surprised by the lack of an appropriate compilation. After considerable effort in searching the literature, the Committee concluded that no list of chemicals was available in the published literature that included all the known automotive-exhaust chemicals and the rates of their emission from diesel or gasoline engines.

In developing its own list of chemicals emitted from diesel and gasoline engines, the Committee examined approximately 250 published papers. Of these, only 16 contained information usable by the Committee in preparing the list of several hundred (Appendix A) considered in this feasbility study. The Committee recognizes that many chemicals emitted in the vapor-phase in exhaust from engines can undergo transformation, both photochemically and in "dark" reactions in the atmosphere, to form biologically potent chemicals. None of the latter chemicals has been considered; only those reported to be present in exhaust have been dealt with in this study. Perhaps this Committee's efforts in starting such a list of chemicals can be continued, so that each listed substance and the atmosphere transformation products can be evaluated more completely in future studies.

Because the number of chemicals in the list is very large, the Committee made a preliminary data-base search (covering 1980-1982; see below for pre-1979 data) of the National Institute for Occupational Safety and Health (NIOSH) Registry of Toxic Effects of Chemical Substances (RTECS) and the NRC Toxicology Information Center (NRCTIC). The preliminary search covered most of the chemicals in the list and requested only the numbers of bibliographic records containing toxicologic or epidemiologic information on each chemical. This preliminary screening sought to find chemicals on which there were at least five bibliographic records of toxicologic or epidemiologic information. This search revealed 14 chemicals in NRCTIC and 50 in RTECS. Further searching was done in the NRCTIC card catalog for information on pre-1979 nonacute studies. TOXLINE was later searched for any chemicals with at least five bibliographic records of toxicologic (nonacute) information. If the retrieval was of manageable size (a small number of bibliographic records), then the titles, authors, and references were printed out; if the number of records was too large, the search was repeated with the limiting search terms "diesel" and "review article," and the titles, authors, and references were printed out.

The Committee reviewed the results of the RTECS, NRCTIC, and TOXLINE searches and compiled an empirical candidate list of 23 compounds. These chemicals are listed in Table 1. The Committee then evaluated the relevant epidemiologic and long-term toxicologic information on each for the purpose of assessing risk.

It should be emphasized that the Committee's efforts were directed toward determining the feasibility of performing a risk assessment for chemicals present in vehicle exhaust and that the Committee operated under severe time constraints. There was no exhaustive attempt to review all the published literature; what was asked was whether sufficient information existed on human health and magnitudes of exposure to each of these chemicals that might be used in risk assessment.

The toxicologic information on the 23 chemicals was evaluated on the basis of various criteria: relevant toxicity data must be available; the chemicals must be present in engine exhaust in more than trace quantities (i.e., they must appear as more than unquantifiable spikes on the chromatogram); and a chemical chosen must be representative of a chemical class.

The bulk of the literature available reported on short-term testing, primarily in vitro and LD_{50} studies. Some long-term carcinogenesis assays were found but most were studies of effects on rodent skin. Notable for their almost complete absence were long-term studies that evaluated any disease endpoints other than cancer. The Committee wishes to go on record as being concerned about this lack of information. Studies of other disease end points, such as emphysema, would be of great value in assessing risk. The Committee agreed that information on formaldehyde and benzanthracene appeared to be sufficient for assessing risk to human health, but no epidemiologic information was found on any of the other 21 chemicals.

Table 1

Pruning Sequences for 23 Candidate Chemicals Chosen for Review of Available Toxicologic Literature

Compound	Rank[a]	Pruning Sequence[b] 1	2	3
Formaldehyde	1	*	*	*
Benz[a]anthracene	2	*	*	*
Fluoranthene	3			
Pyrene	4	*	*	
Alkylfluoranthenes	5	*	*	
Methylpyrenes	6			
Cyclopenta[c,d]pyrene	7	*		
Furfural	8			
Anthracene	9	*		
9,10-Dimethylanthracene	10	*		
Triphenylene	11			
Phenanthrene	12	*		
2-Hydroxybiphenyl	13	*	*	
Chrysene	14	*	*	c
Acrolein	15	*	*	*
Crotonaldehyde	16	*		
Isobutyraldehyde	17			
Butyraldehyde	18			
2-Nitrofluorene	19	*	*	c
Ethylene	20			
4-Nitrobiphenyl	21			
Ethyl nitrite	22			
2,5- or 2,7-dinitrofluorenes	23			

[a]The rank order in Table 1 was based on a consensus of the Committee before its literature review and was aimed solely at guiding the NRC information specialists as to the order in which they should search.

[b]Compounds remaining as candidates.

[c]Strong consideration was given to inclusion in pruning sequence 3.

After a review of the literature on all 23 compounds (summaries of toxicologic findings in the published literature are given later in this report), all but 13 were eliminated (pruned from the list) because of lack of emission data or adequate toxicity information other than that from short-term bacterial or in vitro studies. These 13 are shown as pruning sequence 1 in Table 1. For at least four of them, the only available data beyond results of short-term bacterial and in vitro studies were from long-term skin-cancer studies. The Committee judged that the results of these skin studies were of questionable value for use in quantitative risk assessment, because of the uncertainty of how to extrapolate skin dose to inhalation dose, although it did identify them as carcinogens. There were also data from skin-tumor studies that had used repetitive doses of some of these chemicals. These were judged not to be useful in quantifying cancer risk, because of the lack of information on inhalation exposure to the same chemicals. However, the Committee did consider two approaches that could be used in the future for extrapolating skin dose to inhalation dose. One approach would have been to seek data on skin tumorigenicity for comparison with a known carcinogen shown by inhalation exposure to cause pulmonary tumors (e.g., a compound whose potency in producing skin and pulmonary tumors had been studied, such as benzo[a]pyrene). The second approach would have been to search the literature for compounds that had been studied by both inhalation and skin-painting (e.g., bischloromethyl ether), to see whether there was any general basis for connecting skin dose-effect relations to inhalation dose-effect relations. There were many problems with both approaches, and neither was considered suitable for use in this study. Both, however, warrant consideration for possible adaptation and use in future studies of risk comparisons.

Elimination of chemicals on which there was inadequate information reduced the number of candidate chemicals to eight (see pruning sequence 2 in Table 1); these were reviewed for their representativeness of the classes of chemicals present in engine exhaust and were found to provide a reasonable approximation. Further study revealed that the available data on these chemicals were mostly from long-term repetitive skin-cancer studies and long-term feeding studies with negative results. In the judgment of the Committee, there was sufficient positive information for use in formulating a risk assessment only on acrolein, benz[a]anthracene, and formaldehyde and perhaps 2-nitrofluorene and chrysene, although the latter two were eliminated in the final analysis (see pruning sequence 3 in Table 1).

DISCUSSION

SHORT-TERM BIOLOGIC TESTING

Several hundred chemicals have been identified in gasoline- and diesel-engine exhaust (see Appendix A). It is impossible to test and evaluate each one for its adverse biologic activity. Although much biologic testing has been done, the additional tests needed to measure various disease end points are costly and time-consuming. Therefore, rapid biologic testing methods--e.g., the Salmonella/microsome assay--have been used to identify activity in fractions of extracts of particulate matter collected from engine exhaust. The results of mutagenicity assays or other short-term biologic tests have been and continue to be used to identify biologically active subfractions, so that chemists analyzing engine exhausts can direct their efforts to separating and identifying the chemicals responsible for specific mutagenic activity. The data on the fractions of individual exhaust components vary widely in completeness of animal toxicity-test results.

There has been some question as to the degree of confidence to be attached to results of short-term screening tests that detect a variety of genetic end points, in the absence of other, more conclusive evidence. A recent NRC report (NRC, 1983a) concluded that the number of chemicals to be screened for mutagenic activity is so great that it is important to have several rapid, sensitive, inexpensive tests available, e.g., tests that use microorganisms and cell cultures. The report stated that the determination in mice or other mammals that a substance is a mammalian mutagen constitutes a strong presumption that it is mutagenic in man; it is a "presumed mammalian mutagen" only if results are positive in two or more screening tests that involve different end points or divergent test systems. Classification as a presumed mammalian mutagen may itself be sufficient information for a qualitative or comparative risk-benefit evaluation.

Rapid tests in microorganisms for genetic end points are used to identify the so-called biologically active fractions of particulate extracts from engine exhaust. The results of these tests have guided researchers as to which subfractions of particulate extracts should be selected for the expensive analytic work needed to identify chemicals in the exhaust mixture for sorting out those suspected of biologic activity, and for assigning priorities for further toxicity testing.

BENZENE AND ALKYLBENZENES

Chemicals were removed from the Committee's large initial list for reasons other than lack of bibliographic records of information in the literature. For example, there is more than sufficient information on benzene and the alkylbenzenes for quantitative risk assessment. But the extent to which vehicle use contributes to ambient-air contamination due to these chemicals depends almost totally on their concentrations in unburned fuel and on their evaporation from storage facilities or transport and transfer systems, rather than on their concentrations in engine exhaust. The concentration of benzene is much higher in gasoline than in diesel fuel. Accordingly, a risk assessment concerning diesel vs. gasoline fuels that considered the health effects associated with benzene would not be concerned with engine emission and therefore could give misleading results regarding the source of the exposure that was erroneously attributed to vehicle exhaust.

POLYCYCLIC AROMATIC HYDROCARBONS AND ALDEHYDES

Much is known about the potential human health effects of some chemicals identified in engine exhaust, such as the aldehydes and polycyclic aromatic hydrocarbons (PAHs), but the data on many of them are inadequate, inconclusive, or conflicting. It is therefore difficult to use those data in constructing an approach to risk analysis. It is known that many PAHs bind to DNA, RNA, histones, etc., but the importance of this binding has not been fully assessed, and the specific binding sites have rarely been tested in a manner capable of yielding an understanding of dose-response relations.

FOUR MAIN PROCESSES OF RISK ASSESSMENT

For risk to occur, a subject must be exposed to a chemical, it must be known that the chemical is toxic, and the magnitude, duration, schedule, and route of exposure must be known and considered relevant. (See more detailed discussions on approaches to evaluating health effects for purpose of risk assessment in Appendix B.)

A National Research Council committee has recently considered the current practice of risk assessment (NRC, 1983b) and has described the following four processes contained in some or all assessments of risk:

- Hazard identification: The process of determining whether exposure to an agent causes an increase in the incidence of a given adverse health effect. The Committee on Vapor-Phase Organics identified a potential human health hazard in exposure to vapor-phase organic substances emitted in diesel- and gasoline-engine exhaust, in that some of the chemicals emitted are mutagenic or carcinogenic.
- Dose-response assessment: The process of characterizing the relation between dose and incidence of an adverse health effect in exposed populations and estimating the incidence of the effect as a function of exposure. As discussed in more detail below, the Committee concluded that the

number of chemicals present in the vapor phase of gasoline or diesel exhaust on which there was sufficient information for a dose-response assessment were too small for the purposes of this task.

- Exposure assessment: The process of measuring or estimating the intensity, frequency, and duration of human exposure to the hazardous chemical. Some of the available information suggests that exposure assessment might be based on data on carbon monoxide as a surrogate for other chemicals in exhaust on which there are no quantitative data. However, the data are insufficient, for some chemicals, to permit dose-response assessment.
- Risk characterization: The process of using the above information to estimate the incidence of the adverse health effect in a given population described in the exposure assessment. In view of the deficiencies in the data base for dose-response and exposure assessment, a risk characterization of vapor-phase organic emission could not be performed.

The paucity of the information available on each chemical is clearly seen in Appendix A. For most of these chemicals, insufficient information is available on emission rates by engine type for use in making broad comparisons, but there is some information on emission from one engine type or another). This is particularly unfortunate, because it precludes comparisons of potential exposure to the emission by engine type. In many cases small changes in analytic procedures or in data recording would have led to the production of information useful for exposure assessment, for health-hazard assessment, and for other elements of abatement or control decision-making. The data in Appendix A show a wide range of reported emission rates in the few instances in which data are available from more than one laboratory. The differences in reported emission rates may have resulted from a lack of uniformity in power train, engine cycle, running time, or temperature or from a host of other procedural variables. This again points out the great need for a thorough evaluation of vehicle emission based on a carefully defined and realistic approach that can be applied consistently in different laboratories.

EXPOSURE MODELING

Although the Committee was not asked, as part of its feasibility study, to calculate exposure data from emission data, it did seek to explore whether current technology would permit such calculations. Are there methods for converting vehicle emission data to human exposure estimates? The Committee sought the assistance of David P. Choch of General Motors Research Laboratories, who presented information on several exposure models that have been reported in the literature. In one approach that appears practical, carbon monoxide would be used as a marker (surrogate) for other chemicals emitted in exhaust, and a mathematical model would be used to calculate concentrations of a suspect chemical expected at a given location distant from the roadway. (See Appendix C for further elaboration and an illustrative example of exposure modeling.) Information on the relation between the concentration of emitted carbon monoxide and ambient concentrations of the other emitted compounds in exhaust is available (although it has not been collected or evaluated in this study for this use). Such a relation (with appropriate conversion factors) could serve as a basis for estimating ambient

concentrations that would probably be accurate to within a factor of 2-3. It would also be of value in calculating an average concentration to which a known subpopulation of the United States might be exposed, with an eye to estimating the broader potential health hazard. Total risk could then be estimated by using population density patterns or by using existing ambient-air monitoring data or current studies that measure carboxyhemoglobin concentrations in nonsmokers.

ADEQUACY OF TOXICOLOGIC INFORMATION

The Committee found that there is inadequate toxicologic information on representative individual chemicals identified in the vapor phase of either diesel- or gasoline-engine emission that it judged could be used for quantitative risk assessment based on quantitative estimation of the adverse health and other effects of exposure to vapor-phase components in exhaust. Thus, the Committee could not find data that it deemed adequate or sufficiently reliable on five to 10 chemicals, as specified in the statement of task, for use in a quantitative or qualitative risk assessment. It must be emphasized that the Committee, during this feasibility study, considered all the chemicals listed in Appendix A in the hope of finding worthy candidates for use in any followup study wherein risk assessment would be attempted. No attempt was made during this study to evaluate the quality of information reported in the literature; the objective was merely to identify the types and quantity of information available. Furthermore, until the last pruning sequence in the review of the candidate chemicals (Table 1), the Committee included consideration of all of them, even if the reported information showed no effects. The results were disheartening, in that they implied that, despite the major public and regulatory interest in chemicals emitted in diesel- and gasoline-powered automotive exhaust, there was still insufficient information for quantitative risk assessment of even five of the several hundred vapor-phase chemicals identified in exhaust. Clearly, it is necessary to develop far more information that identifies and characterizes the potential adverse effects of these very important chemicals emitted into the atmosphere, if risk assessment of individual chemicals is to be used as a tool.

The Committee emphasizes that, because of the time constraints imposed, it did not examine the literature on all the chemicals listed in Appendix A. It is conceivable, although unlikely, that references to research that could be used in quantitative risk assessment were missed. The choices made in the sampling strategy had limitations that were mandated by time and resources. Therefore, the sampling strategy cannot be viewed as a rigorous approach to a search of all the available literature. Strategies to determine needs and priorities for toxicity testing are being developed by another NRC committee (NRC, 1983c) and could have application in selecting future studies of chemicals emitted in engine exhaust. However, one does not need a rigorous statistical treatment of this information to conclude that there is a serious dearth of information on various chemicals of great significance for abatement and control decision-making by regulatory agencies, the public, and industry.

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SUMMARY OF TOXICOLOGIC FINDINGS IN THE PUBLISHED LITERATURE

The following summaries of toxicologic information were used by the Committee in determining the availability of relevant data found to be usable for assessment of risk. There are no summaries for methylpyrenes and the dinitrofluorenes, because the bibliographic resource material was not considered relevant to this study.

CYCLOPENTA[c,d]PYRENE

Cyclopenta[c,d]pyrene (CPP) has been known to be present in organic combustion products for decades, but only recently has it undergone testing for carcinogenicity and mutagenicity. Interest in this compound stems partly from observations that indicate that, although it is similar to benzo[a]pyrene in mutagenicity in Salmonella typhimurium, it is a much less potent inducer of mouse skin tumors (Kaden et al., 1979; Cavalieri et al., 1981; Wood et al., 1980). Gold and Eisenstadt (1980) suggested that 3,4-epoxycyclopenta[c,d]-pyrene was the major microsomal mutagenic metabolite, according to studies in rat liver. Using perturbation molecular orbital calculations, Fu et al. (1980) predicted that cyclopenta-polycyclic aromatic hydrocarbons may constitute a greater biologic hazard than some other polycyclic aromatic hydrocarbons.

The reason for the apparent discrepancy between the degree of carcinogenicity and the bacterial mutagenicity of CPP is unclear. Raven et al. (1982) noted that the relationship between tumor-initiating potency and mutagenic activity, compared with benzo[a]pyrene, correlated more closely if mutagenesis was tested in a mammalian cell-mediated assay using V79 Chinese hamster cells. Mutagenicity of CPP in mammalian cell systems was also noted by Nesnow et al. (1981).

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9,10-DIMETHYLANTHRACENE

9,10-Dimethylanthracene (9,10-DMA) was originally identified as a carcinogen by Kennaway et al. (1942), who used repetitive skin-painting to demonstrate the tumorigenicity of this compound in C3H mice. The data showed a slight trend to increased pulmonary adenomas in this early study. More recently, Wislocki et al. (1982) evaluated the ability of 9,10-DMA to initiate skin tumors in mice in a study in which a single dose of 400 or 1,000 nmol of hydrocarbon was followed by 31 wk of promotion with phorbol myristic acetate. Although 9,10-DMA-initiated mice had a somewhat higher incidence of papillomas than those tested with acetone or anthracene, the difference was not statistically significant.

9,10-DMA has been evaluated in a variety of short-term assays with differing results. The findings include a positive result in the BHK cell transformation assay (Strobel and Greb, 1981); a positive result in the Salmonella/microsome assay in the presence of S 9 fraction (Andrews et al., 1978); negative results in mutagenicity tests, as indicated by a lack of increased petite frequencies in Saccharomyces cerevisiae (Gillson et al., 1979); and a lack of induced sperm-head abnormalities in mice given daily intraperitoneal injections of 9,10-DMA at 50, 100, 250, or 500 ng/kg for 5 d (Topham, 1980). This inconsistency in response was also observed by Purchase et al. (1978) in a study comparing six short-term tests for detecting organic chemical carcinogens: 9,10-DMA was negative in four tests (mammalian BHK

21-cell transformation, skin response to subcutaneous implant, degranulation of rat liver rough endoplasmic reticulum, and reduction of tetrazolium red by mouse skin) and positive in two short-term tests (the Salmonella/microsome assay and the suppression of mouse skin sebaceous gland growth). Probst et al. (1981) found 9,10-DMA to be negative in a modified Salmonella/microsome assay, but positive in a test evaluating chemically induced unscheduled DNA synthesis in primary rat hepatocyte cultures. Accordingly, 9,10-DMA can be considered a weak mutagen and carcinogen.

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TRIPHENYLENE

Triphenylene has been tested for mutagenicity in comparison with other polycyclic aromatic hydrocarbons by a number of investigators. Using an in vitro human lymphoblast mutation assay, Barfknecht et al. (1982) reported that triphenylene had 4% of the mutagenic potential of benzo[a]pyrene. Triphenylene was mutagenic in Salmonella typhimurium in activated systems (Mossanda et al., 1979; Hermann, 1981) and was found to have 13% of the activity of benzo[a]pyrene (Hermann, 1981). When they were tested together, triphenylene was found to inhibit the mutagenicity of benzo[a]pyrene slightly. Triphenylene epoxides were noted to be mutagenic by Wood et al. (1980).

Topical application of triphenylene to neonatal rats resulted in the induction of aryl hydrocarbon hydroxylase and 7-ethoxycoumarin-O-deethylase activity in liver, but not skin (Mukhtar et al., 1982).

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ANTHRACENE

Anthracene has been tested for mutagenicity in a variety of short-term tests with generally negative findings (Greb et al., 1980; Topham, 1980; Lake et al., 1978; Simmon et al., 1979; Salamone et al., 1979). Purchase et al. (1978) found that anthracene was positive in a test based on the degranulation of rat liver endoplasmic reticulum in vitro, but was negative in five other short-term tests.

Anthracene has been reported to be negative (Salaman and Roe, 1956) and minimally positive (Scribner, 1973) in long-term initiation-promotion tests in mouse skin.

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PHENANTHRENE

Phenanthrene has been studied for mutagenicity in bacterial and mammalian systems, with generally negative results (Simmon et al., 1979; Greb et al., 1980; Maksuoka et al., 1979; Lake et al., 1978; and LaVoie et al., 1981). However, Oesch et al. (1981) reported on a bacterial mutagenesis system in which use of a variant of the usual rat hepatic metabolizing system resulted in positive findings. The authors suggested that there are two activation pathways in phenanthrene metabolism. No effect of phenanthrene on bacterial ciliary activity in vitro was observed by Pettersson et al. (1982).

Phenanthrene was tested for carcinogenicity in mouse skin as long ago as 1924, with generally negative restuls. Relatively recent studies include the report by Salaman and Roe (1956) of a slight, but apparently not statistically significant, increase in mouse skin tumors after treatment with 10 applications (three a week)--for a total of 0.54 g--followed by tumor promotion with croton oil. No skin tumors were observed by LaVoie et al. in 20 mice initiated with 1 mg of phenanthrene and then promoted with phorbol myristic acetate. However, Scribner (1973) used a similar approach and reported that phenanthrene was a weak tumor initiator in mouse skin. Buening et al. (1979) evaluated newborn mice given intraperitoneal injections of phenanthrene on the first, eighth, and fifteenth days of life. No increase in hepatic or pulmonary tumors was observed, but there was a 6% incidence of lymphomas in female mice, compared with none in the control group.

These contradictory findings suggest that phenanthrene is at most weakly mutagenic and carcinogenic.

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2-HYDROXYBIPHENYL (o-PHENYLPHENOL)

2-Hydroxybiphenyl (o-phenylphenol) has a wide variety of uses as a fungicide in commercial and household products. It has been identified in the volatile phase of diesel exhaust (Hampton et al., 1982). The compound has a relatively low order of acute toxicity in animals, and extensive skin studies on human subjects have indicated that it is neither an irritant nor a skin sensitizer at concentrations up to 5% in oil (Gosselin et al., 1976). A more recent report (Adams, 1981) suggested that contact sensitivity may occasionally occur.

A 2-yr feeding study in rats and a 1-yr feeding study in dogs were carried out by Hodge et al. (1952). Diets containing 2-hydroxybiphenyl at 0.02% or 0.2% were without effect in rats. At a dietary concentration of 2% for 2 yr, there was slight depression of growth and dilatation of kidney tubules. No other effects were reported. Dogs receiving 0.02, 0.2, and 0.5 g/kg for 1 yr showed no adverse effects. Currently there is a carcinogenesis bioassay program within the National Toxicology Program.

Ogata et al. (1978) found 2-hydroxybiphenyl to be maternally toxic and fetotoxic, but not teratogenic in mice. John et al. (1981) reported that 2-hydroxybiphenyl was not embryotoxic or teratogenic in rats at up to 700 mg/kg per day. Shirasu et al. reported no dominant-lethal mutations after oral administration at 100 or 500 mg/kg per day to male C3H mice. They also reported negative results in a series of mutagenic studies using B. subtilis H17 and M45, E. coli WP2 her, and S. typhimurium TA 1535, 1537, 1538, 98, and 100.

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ISOBUTYRALDEHYDE (2-METHYLPROPANAL)

Isobutyraldehyde has a relatively low order of skin irritation in the rabbit, whereas eye irritation is moderate (grade 5 on a relative grading scale with a maximum of 10) (Smyth et al., 1954).

Isobutyraldehyde was mutagenic in 4 of 5 Salmonella strains used in detecting base substitution and nonmutagenic in all frame-shift test systems (McMahon et al., 1979). It had no effect on membrane permeability of human fibroblasts studied in vitro (Thelestam et al., 1980). No long-term studies are available.

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CHRYSENE

Chrysene is a polycyclic aromatic hydrocarbon found in the vapor phase in diesel exhaust (0.032 mg/mi). It is present in relatively high concentrations in organic particulate matter in the atmosphere--at 150-490 µg/g of organic matter in six American cities, 200-533 µg/g in three German cities, and 42-119 µg/g in dust samples from an automobile tunnel (International Agency for Research on Cancer (IARC), 1973). Chrysene is also present in tobacco smoke (Florin et al., 1980).

Carcinogenicity studies with skin application of chrysene, generally using chrysene in solution at 0.3% or less, have been both negative and positive in the older literature. In more recent studies, Wynder and Hoffmann (1959) applied 1% chrysene in acetone three times a week and produced papillomas in 9 of 20 and carcinomas in 8 of 20 female Swiss mice. Van Duuren et al. (1966) produced no tumors with a single application of 1 mg of chrysene in acetone; however, the same treatment initiated carcinogenicity when it was followed by repeated treatment with croton resin, resulting in papillomas in 16 of 20 mice and carcinomas in 2 of the 20.

Steiner and Falk (1951) produced sarcomas in 4 of 50 C57BL mice that received subcutaneous injections of 5 mg of chrysene in tricapryline. Steiner (1955) gave 40-50 C57BL mice 5 mg of chrysene in tricapryline; 22 survived 150 d, and 5 developed sarcomas.

No tumors appeared in 50 mice observed over 50 wk after an intraperitoneal injection of 2 mg of chrysene in lead (Bottomley and Twort, 1934).

Female CD-1 mice (7-8 wk old) were treated topically with a single application of chrysene or chrysene derivatives at 0.4, 1.25, or 4.0 µmol/mouse (Levin et al., 1978). Beginning 7 d after application, all animals received applications of 12-o-tetradecanoylphorbol-13-acetate twice a week for 25 wk. For the three dosages of chrysene, tumor incidences were 25, 43, and 52%, respectively, compared with 7% in control animals. Chrysene 1,2-dihydrodiol had considerably greater activity than the parent compound.

Buening et al. (1979) gave newborn Swiss-Webster mice intraperitoneal injections of 0.2, 0.4, and 0.8 µmol of chrysene on the first, eighth, and fifteenth days of life. Studies were terminated when the animals were 38-42 wk old. Lung adenomas developed in 15% of control animals. Chrysene had

little or no effect on the lung, but resulted in a 20% incidence of hepatic tumors in male mice. Several diol-epoxide derivatives of chrysene produced lung tumors in 75-95% of male mice; similar derivatives of the cis-trans configuration were relatively inactive. Wood et al. (1980) found an 80% incidence of skin tumors in mice when 2.5 μmol was applied to the skin and followed by applications of TPA (T-phorbol ester) tumor promoters twice a week.

Thus, chrysene has been shown to produce skin tumors in mice after repeated application or after a single application followed by application of promoters. Subcutaneous injection has also produced tumors in mice. It has apparently not been tested by other routes.

Chrysene has been tested for mutagenicity in several systems. It has mutagenic activity in the human lymphoblast assay (Barfknecht et al., 1982) when a rat liver microsomal activating fraction is used. Chrysene was also a cell transforming agent in the in vitro test system using BHK 21/CL 13 cells (Greb et al., 1980). It was mutagenic in strain TA 100, but not strain TA 98, in the Salmonella test (Okamoto et al., 1978).

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ETHYLENE

Ethylene has low acute toxicity, being without effect in rats at 10,000 ppm (11.5 g/m^3) for 4 h. A similar exposure is acutely hepatotoxic in rats pretreated with Aroclor 1254. Thus, stimulation of microsomal metabolism apparently increases the hepatotoxic response (Conolly and Jaegen, 1979).

Ethylene is considered a simple asphyxiant; that suggests that it has essentially no physiologic effect other than to deplete the oxygen supply in large exposures (ACGHIH, 1982). No case reports or epidemiologic studies are available.

Aroclor pretreatment increased the conversion of inhaled ethylene to CO_2 and urinary metabolites and increased the quantities found in tissues 36 h after a 5-h exposure at 10,000 ppm (Guest *et al.*, 1981).

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4-NITROBIPHENYL

4-Nitrobiphenyl is mutagenic in both the modified Salmonella/ microsome test and the rat hepatocyte culture unscheduled-DNA-synthesis system (Probst et al., 1981). It is also positive in the sister chromatid exchange assay, but requires the presence of a rat liver S-9 fraction (Nachtman and Wolff, 1982). El-Basyoumy et al. (1981) reported 4-nitrobiphenyl to be highly mutagenic in Salmonella strains TA 98 and TA 100, both with and without metabolic activation. Similar findings have been reported by McCann et al. (1975). Thus, there is a considerable body of evidence that indicates that 4-nitrobiphenyl is mutagenic.

Deichmann et al. (1958) produced bladder tumors in two of four dogs given 300 mg of 4-nitrobiphenyl three times a week for 33 mo (total dose, approximately 10 g/kg). A later study of Deichmann et al. (1965) was negative in six dogs receiving lower doses of 4-nitrobiphenyl (total dose, approximately 0.77 g/kg). Laham (1960) reported that 4-nitrobiphenyl was converted to an active carcinogen. Nehleke and Nestel (1967) reported that anaerobic incubation of 4-nitrobiphenyl with rat liver enzymes resulted in the conversion of substantial quantities to 4-aminobiphenyl, known to produce bladder tumors in animals. There are no human case reports or epidemiologic studies related directly to carcinogenicity.

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CROTONALDEHYDE

Crotonaldehyde is a direct mutagen in Salmonella typhimurium TA 100 in a modified Salmonella/microsome assay (Lutz et al., 1982; Lijinsky and Andrew, 1980). Intraperitoneal injection of 1.0 mg/animal caused chromosomal damage at all stages of spermatogenesis in male mice; the results were the same when crotonaldehyde was administered for 1 mo in the drinking water at 0.2 g/L (Moutschen-Dahmen et al., 1975, 1976; Auerbach et al., 1977).

Crotonaldehyde is very active in causing ciliostasis in chicken trachea organ cultures (Pettersson et al., 1982). It inhibits chemotaxis and adherence of polymorphonuclear leukocytes to nylon fiber columns; that is indicative of membrane alterations (Bridges et al., 1980). Inhalation of crotonaldehyde at 2.4-5 ppm decreases respiration and heart rate in male rabbits (Ikeda et al., 1980).

In humans, inhalation of air containing crotonaldehyde at 12 mg/m^3 (4.1 ppm) for 10 min led to lacrimation within 30 s and irritation of all exposed mucosal surfaces (Sim and Pattle, 1957).

An increased prevalence of malignant tumors in workers exposed to a mixture containing crotonaldehyde, other aldehydes, and aliphatic compounds was reported by Bittersohl (1975) and the NRC (1981).

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BUTYRALDEHYDE

Butyraldehyde is nonmutagenic in the standard Salmonella/microsome assay with Salmonella typhimurium TA 98, 100, 1535, and 1537 with or without S-9 from Araclor-induced rats (Florin et al., 1980). In a modified assay using 15-min preincubation of bacteria with butyraldehyde followed by plating with or without S-9 from rats, Sasaki and Endo (1978) also reported this compound to be nonmutagenic in TA 100 and TA 98. It was found to cause chromosomal damage and meiotic anomalies at all stages of spermatogenesis in mice a month after a single intraperitoneal injection of 1.0 mg/animal or after daily consumption of drinking water containing 0.2 g/L for a month (Opdyke, 1979; Moutschen-Dahmen, 1975, 1976).

In other in vitro studies, butyraldehyde caused permeability changes in human diploid embryonic fibroblasts (Thelestam et al., 1980), inhibited oxygen consumption in hamster brown fat cells stimulated by norepinephrine (Pettersson et al., 1980), and induced erythroid differentiation in proerythroblastoid murine erythroleukemic cells (Malinin and Ebert, 1980).

Inhalation exposure of humans to butyraldehyde at 230 ppm for 30 min was nonirritating (Sim and Pattle, 1957; NRC, 1981, see p. 229).

Butyraldehyde was implicated as an etiologic factor in human cancer by Bittersohl (1975).

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FURFURAL

Furfural is weakly mutagenic in the standard Salmonella/microsome assay using TA 100 (Loquet et al., 1981); that activity was not increased by addition of S-9 (Zdzienicka et al., 1978). Auerbach et al. (1977) reported furfural to be slightly radiomimetic in Vicia faba roots. The compound was found to be clastogenic in Chinese hamster ovary cells, where it produced a relatively high frequency of chromatid breaks and chromatid exchanges. These effects increased when S-9 was included in the 3-hour exposure to 10-40 mM furfural (Stich et al., 1981).

Inhalation studies by Ikeda et al. (1980) showed no effects on respiration or heart rate of male rabbits exposed to furfural at 2 ppm for 10 min. Syrian golden hamsters were exposed to furfural at 20, 115, or 552 ppm 6 h/d, 5 d/wk, for 13 wk via inhalation. The highest concentration produced eye and nose irritation, slight growth retardation, and atrophy with hyperplasia of the olfactory epithe[illegible]um in the nasal cavity. At 115 ppm, only atrophy and hyperplasia we[illegible]

observed (Feron et al., 1979). Intratracheal instillation of 1.5% furfural in 0.2 ml of 0.9% NaCl once a week for 36 wk in Syrian golden hamsters resulted in irritation effects, such as slight hyperplasia of the tracheobronchial epithelium, alveolar metaplasia, and peribronchiolar adenomatoid proliferation of the bronchioalveolar epithelium (Feron, 1972). The same experimental protocol using combined intratracheal instillation of furfural (1.5%) and benzo[a]pyrene (about 1 mg) resulted in earlier development of irritation effects, a shorter latent period for tracheobronchial tumors, the induction of a few more bronchial and peripheral squamous cell carcinomas, and the induction of considerably more peritracheal sarcomas than when benzo[a]pyrene was administered without furfural. These data point to a cocarcinogenic effect of furfural on the respiratory tract of hamsters.

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ETHYL NITRITE

Ethyl nitrite, which is the ethyl ester of nitrous acid, was shown by Ehrenberg et al. (1980) to be mutagenic in Salmonella typhimurium. The observed mutagenic activity was greater than that of sodium nitrite under identical experimental conditions. In E. coli Sd-4, the

mutagenic activity of ethyl nitrite was increased by primary amines, and the frequency of chlorophyll mutations was increased (although not to a statistically significant degree) in barley seeds treated with this compound. It is possible that ethyl nitrite is hydrolyzed to nitrous acid, a compound capable of forming nitrosating species that can react with primary amines to form clastogenic, mutagenic, and carcinogenic N-nitroso compounds (Ishidate and Odashima et al., 1977.)

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ACROLEIN

In a modified Salmonella/microsome assay using liquid suspension, acrolein was found to be a potent direct mutagen in S. typhimurium TA 100 (Lijinsky et al., 1980; Lutz et al., 1982). The mutagenic activity of acrolein and other unsaturated aldehydes and similar compounds is correlated with the degree of electrophilicity of the carbon and is decreased by addition of S-9 (Lutz et al., 1982).

In other in vitro studies, Pettersson et al. (1982) found acrolein to be very active in causing ciliostasis in chicken trachea organ culture, and Bridges et al. (1980) reported that acrolein causes a dose-dependent inhibition of adherence of polymorphonuclear leukocytes to nylon fibers and of chemostasis; these observations suggest membrane damage.

Rat embryos and yolk sacs treated in vitro with acrolein were inhibited in growth and differentiation (Schmid et al., 1981). No evidence of teratogenicity was observed in rat embryos cultured in vitro in the presence of acrolein (Mirkes et al., 1981) or in chicken embryos from eggs treated on day 3 with acrolein and examined on day 4 of incubation (Kankaanpaa et al., 1979). However, acrolein produced teratogenic effects--such as hydrocephalus, open eyes, and cleft palate--in embryos from pregnant rats given injections on day 13 of gestation and examined on day 20 (Hales, 1982).

A 52-wk inhalation study using hamsters did not find acrolein to be carcinogenic (Feron and Kruysse, 1977). Subcutaneous injection of acrolein into mice did not result in tumors at the site of injection, nor was acrolein found to exhibit any appreciable tumor-initiating activity (NRC, 1981, p. 237).

In humans, acrolein is predominantly an eye and respiratory irritant. Its effects in humans have been summarized previously (NRC, 1981, pp. 238-241).

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PYRENE

Nikonova (1977) injected 12 mg of pyrene into pregnant mice and found no significant incidences of mammary gland or lung tissue tumors. Similar injections of benzo[a]pyrene produced a lung cancer incidence of 76.8%, a hepatic tumor incidence of 23.3%, and a mammary gland tumor incidence of 36.4%.

LaVoie et al. (1979) found that pyrene was inactive as a mutagen in the Salmonella/microsome assay.

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2-NITROFLUORENE

Miller et al (1962) found that 2-nitrofluorene can induce a high incidence of papillomas and carcinomas of the forestomach. Morris et al. (1950) found that it is carcinogenic in rats, inducing distant tumors at various sites either after ingestion (at 500 ppm in food for 23 wk) or after painting (2% in acetone solution, three times a week for 6 mo and thereafter 6 drops three times a week for 16-21 mo). An average of 0.53 tumor per rat was observed for 2-nitrofluorene, compared with 0.82 tumor per rat for 2-aminofluorene. More tumors were induced by painting with 2-nitrofluorene than by its ingestion, whereas 2-aminofluorene produced more tumors by ingestion.

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FLUORANTHENE

Thilly (1982) found that fluoranthene accounted for 30% of the total mutagenicity of a diesel particulate extract tested in human lymphoblasts. Fluoranthene was approximately 30 times more mutagenic than benzo[a]pyrene when tested in Salmonella typhimurium strain TA 677 (Kaden et al., 1979).

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ALKYLFLUORANTHENES

1-Methylfluoranthene and 7-methylfluoranthene are noncarcinogenic; 2- and 3-methylfluoranthenes were carcinogenic on mouse skin and in the hamster respiratory system (LaVoie, 1981; LaVoie et al., 1979a,b). Brunneman and Hoffmann (1976) reported that the tumor-initiating activity of tobacco smoke is due to the presence of 5-methylchrysene, 2-methylfluoranthene, 3-methylfluoranthene, and dimethylfluoranthene. Hoffmann (1972) found that 2- and 3-methylfluoranthenes were active as skin tumor initiators, as were 2,3- and 7,8-dimethylfluoranthenes. 2-Methylfluoranthene was also active as a complete carcinogen.

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CONCLUSIONS

- In this feasibility study, the Committee determined that quantitative risk assessment could probably be applied to only three to five vapor-phase components of diesel exhaust: formaldehyde, benz[a]-anthracene, acrolein, and perhaps 2-nitroflourene and chrysene. Data on the others seem insufficient for detailed quantitative risk assessment, although comparative risk assessment or qualitative risk assessment would be possible.
- Some vapor-phase organic chemicals in diesel- and gasoline-engine exhaust are potentially hazardous. This conclusion is based primarily on the observed mutagenicity of many emission components in short-term tests and their carcinogenicity in animals.
- The risk to the population cannot now be quantitated, owing primarily to a dearth of exposure information on animals and epidemiologic studies pertinent to quantitative risk assessment.
- The available data on individual compounds emitted under different fuel, operating, and exhaust conditions are inadequate.
- The lack of sufficient exposure information to perform quantitative risk assessment on even five (as stipulated in the Committee's task order) of the over 300 vapor-phase compounds identified in fuel exhaust is an unexpected finding. The control of automobile exhaust was an important goal of the Clean Air Act of 1970, and the potential for adverse health effects due to a switch to diesel fuel has been known for about a decade. Such a lack of pertinent information might reflect changes in the priorities with which our country approaches major public-health questions related to the environment.
- The Committee concludes that, in view of the large fraction of the U.S. population exposed to vapor-phase organic chemicals, obtaining the information necessary to assess the risk of vapor-phase fuel exhaust should be given high priority. This research should be focused on crucial subjects on which information is insufficient, particularly (after testing priorities are set through short-term tests) dose-response relations and emission characteristics, to permit an exposure assessment for the population.

RECOMMENDATIONS

- There is a great need for a thorough evaluation of vehicle-exhaust emission with a carefully defined and realistic approach that can be applied in a comparable manner in different laboratories. The data on the chemicals in Appendix A show wide variations in reported emission; thus, it is difficult to make valid comparisons of emission from different vehicle types or to calculate the expected emission for use in exposure assessments.
- A mathematical model should be validated under practical testing conditions to determine the concentrations of selected hazardous chemicals known to be emitted in the exhaust of a variety of vehicle types. It is essential that some accepted procedure be established to calculate and to validate exposure concentrations for use in assessing the risk to human health.
- A procedure should be developed for projecting carcinogenic potency observed in skin-testing to the potency that would be associated with exposure by inhalation. Some practical examples should be used to test the validity of the procedure.
- Recent advances in molecular biology and analytic biochemistry suggest that it will be possible to detect at least some vapor-phase components of diesel- and gasoline-engine exhaust in body fluids. That would be highly useful in providing a biologic indicator of exposure. Furthermore, an assay to measure such end points as DNA adducts in blood cells or other easily obtainable tissue could provide data useful for assessing potential adverse responses in man.

APPENDIX A

REPORTS IN THE PUBLISHED LITERATURE ON VAPOR-PHASE ORGANIC CHEMICALS EMITTED FROM DIESEL OR GASOLINE ENGINES*

Chemical	EMISSION, mg/mi: Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
ALKYL NITROSAMINES				
HYDROCARBONS (UNSAT. AND SAT.)				
Methane	5.3-31.8 (2)	17.5 (1)	106.9 (6)	32.5-120.4 (6)
		23.5-53.1 (2)	410.3 (7)	85.2-273.0 (7)
Ethylene	13.7-79.2 (2)	83.5 (1)	149.1 (6)	8.4-61.8 (6)
	327.5-362.0 (11)	1.8-29.3 (2)	542.4 (7)	18.1-295.7 (7)
Ethane	0.5-6.8 (2)	4.4 (1)	13.3 (6)	4.0-18.2 (6)
		3.9-23.8 (2)	78.8 (7)	4.0-68.0 (7)
Acetylene	1.9-14.4 (2)	42.3 (1)	127.0 (6)	3.8-28.2 (6)
	53.4-63.8 (11)	1.8-4.2 (2)	382.0 (7)	4.0-43.8 (7)
Propylene (propane)[a]	7.2-31.9 (2)	31.7 (1)	78.0 (6)[a]	5.1-37.3 (6)
	102.3-129.4 (2)	6.4-13.2 (2)	229.7 (7)[a]	7.6-28.7 (7)
Propane	0.2 (2)	31.7 (1)		
	0.8-2.3 (11)	N.D. (2)		
Propadiene		1.1 (1)	trace (6)	0.3-1.4 (6)
			12.5 (7)	0.2-0.9 (7)
Methyl acetylene		2.1 (1)	trace (6)	
			29.0 (7)	
Isobutane		3.9 (1)	9.2 (6)	0.3-3.2 (6)
			19.7 (7)	2.0-26.7 (7)
1-Butene	24.8-34.9 (11)			
Isobutylene	14.4-15.9 (11)			
1-Butene; isobutylene		15.8 (1)	19.2 (6)	1.6-17.1 (6)
			9.35 (7)	4.1-49.0 (7)
1,3-Butadiene	11.7-18.1 (11)			
n-Butane; 1,3-butadiene	0.6-1.44 (11)	12.5 (1)	64.7 (6)	5.5-70.4 (6)
			202.3 (7)	14.1-222.4 (7)
trans-2-Butene	4.5-5.6 (11)	3.0 (1)	2.7 (6)	0.5-5.2 (6)
		15.3 (7)	1.3-18.8 (7)	1.3-18.8 (7)
cis-2-Butene		1.7 (1)	5.0 (6)	0.3-29. (6)
			16.9 (7)	1.1-13.2 (7)

*A search of the literature revealed approximately 250 papers that contained some information on vehicle emissions. Only those reported here contained quantitative information on emission rates (milligrams/mile). Note: The operating conditions and temperatures for "vapor phase" may vary in the referenced information presented.

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
3-Methyl-1-butene		1.5 (1)	3.0 (6)	0.1-1.2 (6)
			4.0 (7)	0.3-2.2 (7)
Isopentane	0.6-1.0 (11)	9.7 (1)	31.2 (6)	4.7-79.7 (6)
			125.3 (7)	20.1-201.8 (7)
Pentene-1	17.2-20.9 (11)	0.5 (1)	0.8 (6)	0.1-0.9 (6)
			8.9 (7)	0.5-5.6 (7)
n-Pentane (2-methyl-1-butene)[a]	4.4-5.6 (11)	8.4 (1)	24.9 (6)[a]	4.1-60.8 (6)
			75.8 (7)[a]	7.2-77.6 (7)
trans-2-Pentene		1.4 (1)	1.6 (6)	0.5-2.1 (6)
			12.9 (7)	1.2-9.0 (7)
cis-2-Pentene		1.4 (1)	0.7 (6)	0.3-2.5 (6)
			18.1 (7)	1.9-15.5 (7)
Cyclopentane (3-methyl-1-pentene)[a]		13.2 (1)	43.8 (6)[a]	7.0-48.1 (6)
			9.3 (7)	1.3-71.2 (7)
2,2-Dimethylbutane		(4)	12.1 (7)	
2,3-Dimethylbutane		(4)	4.4 (6)	0.4-6.1 (6)
			21.4 (7)	3.1-24.4 (7)
2,2,3-Trimethylbutane		(4)		
3,3-Dimethylpentane		(4)		
2,2,3-Trimethylpentane		(4)		
2,2,4-Trimethylpentane (isooctane)		(4)	47.0 (6)	9.5-95.0 (6)
			88.7 (7)	9.4-117.9 (7)
2,2-Dimethylhexane		(4)		
2-Methylpentane; 2,3-dimethyl-1-butene[a]			4.1 (6)[a]	0.6-6.8 (6)
			61.3 (7)[a]	5.6-63.8 (7)
3-Methylpentane			1.5 (6)	0.3-3.4 (6)
			35.9 (7)	2.3-41.4 (7)
1-Hexane; 2-ethyl-1-butene[a]			0.7 (6)[a]	0.1-1.5 (6)
			9.3 (7)	0.6-4.5 (7)
2,4-Dimethylpentane			1.8 (6)	0.2-3.0 (6)
			25.0 (7)	1.8-28.6 (7)
3-Methylhexane (cyclohexane (7))[a]			trace (6)	1.3-8.8 (6)
			39.9 (7)[a]	3.3-48.2 (7)
n-Heptane			5.5 (6)	0.4-13.4 (6)
			27.0 (7)	2.1-16.8 (7)
2,4- and 2,5-Dimethylhexane[a]			6.7 (6)[a]	1.2-13.2 (6)
			30.6 (7)[a]	3.8-32.8 (7)
2,3,4-Trimethylpentane			2.9 (6)	1.4-8.2 (6)
			29.4 (7)	8.1-56.0 (7)
2,3,3-Trimethylpentane			2.5 (6)	0.7-2.9 (6)
			13.3 (7)	3.4-13.4 (7)

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)		Gasoline catalyzed (ref)	
2,2,3-Trimethylhexane		(4)				
2,2,4-Trimethylhexane		(4)				
2-Methyl-3-ethylhexane		(4)				
3,5-Dimethylheptane (2,5-dimethylheptane)[a]		(4)	1.6	(6)[a]	0.2-2.5	(6)
			6.9	(7)[a]	0.4-5.3	(7)
2,3,5-Trimethylheptane		(4)				
2,4,5-Trimethylheptane		(4)				
3,3,4-Trimethylheptane		(4)				
3,4,4-Trimethylheptane		(4)				
3,4,5-Trimethylheptane		(4)				
4-Methylnonane		(4)				
Cyclopentane		(4)				
Methylcyclopentane (3-methtrans-2-pentene)[a]		(4)	1.6	(6)[a]	0.3-2.7	(6)
			28.2	(7)[a]	2.8-35.8	(7)
2-Methyl-1-butene	(4)	(4)				
2-Methyl-2-butene	(4)	(4)	10.3	(6)	2.9-44.8	(6)
3-Methyl-1-butene	(4)	(4)				
2-Methyl-1,3-butadiene		(4)				
3-Methyl-1,2-butadiene		(4)				
1-Pentene	(4)	(4)				
2-Pentene, cis	(4)	(4)				
2-Pentene, trans	(4)	(4)				
1,3-Pentadiene		(4)				
2,3-Dimethyl-1-butene		(4)				
2,3-Dimethyl-2-butene		(4)				
3,3-Dimethyl-1-butene		(4)				
2-Ethyl-1-butene		(4)				
2-Methyl-1-pentene		(4)				
2-Methyl-2-pentene		(4)	1.3	(6)	0.3-1.9	(6)
			10.1	(7)	1.4-10.2	(7)
3-Methyl-1-pentene		(4)				
3-Methyl-2-pentene, cis		(4)				
3-Methyl-2-pentene, trans		(4)				
4-Methyl-1-pentene	(4)	(4)				
and/or 3-methyl-1-pentene		(4)				
4-Methyl-2-pentene, cis		(4)				
4-Methyl-2-pentene, trans		(4)				
2- and 3-Hexenes, cis and trans (n-hexane, cis-3-hexene)[a]		(4)	1.4	(6)[a]	0.3-3.9	(6)[a]
			38.3	(7)[a]	1.9-30.2	(7)
2,3,3-Trimethyl-1-butene		(4)				
3,4-Dimethyl-1-pentene		(4)				
3,4-Dimethyl-2-pentene, cis and trans		(4)				
4,4-Dimethyl-2-pentene, cis		(4)				

Chemical	EMISSION mg/mi Diesel (ref)		Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)		Gasoline catalyzed (ref)	
3-Ethyl-1-pentene			(4)				
3-Ethyl-2-pentene			(4)				
2-Methyl-1-hexene			(4)				
3-Methyl-1-hexene			(4)				
4-Methyl-1-hexene			(4)				
5-Methyl-1-hexene			(4)				
5-Methyl-2-hexene, cis and trans			(4)				
2-Heptene, cis or trans			(4)				
Methylcyclohexane				2.2	(6)	1.0-3.7	(6)
				16.5	(7)	1.7-14.0	(7)
2-Methylheptane				9.6	(6)	1.9-16.6	(6)
				25.8	(7)	1.8-23.5	(7)
3-Methylheptane				6.7	(6)	1.3-12.8	(6)
				21.8	(7)	1.1-21.3	(7)
2,2,5-Trimethylhexane				1.4	(6)	0.4-3.3	(6)
				17.7	(7)	2.2-27.9	(7)
n-Octane	6.0	(16)		3.7	(6)	0.8-8.3	(6)
				10.3	(16)[b]		
				18.5	(7)	1.8-11.2	(7)
2,3,5-Trimethylhexane				0.1	(6)	0.1-0.2	(6)
				3.2	(7)	0.4-4.1	(7)
2,4-Dimethylheptane				0.8	(6)	0.1-1.6	(6)
				2.8	(7)	0.2-3.4	(7)
Cyclopentene				4.0	(7)	0.3-6.5	(7)
3-Heptene, cis and trans			(4)				
2,4,4-Trimethyl-1-pentene			(4)	3.2	(7)		
2,4,4-Trimethyl-2-pentene			(4)				
2,3-Dimethyl-2-hexene			(4)				
2,5-Dimethy'-2-hexene, trans			(4)				
2,5-Dimethyl-3-hexene, trans			(4)				
2-Ethyl-1-hexene			(4)				
2-Octene, cis			(4)				
2-Octene, trans			(4)				
2,6-Dimethyl-3-heptene			(4)				
2-Methyl-1-octene			(4)				
1-Decene		(4)					
1-Dodecene			(4)				
Tridecene		(4)					
Tetradecene		(4)					
Pentadecene		(4)					
Hexadecene		(4)					
Heptadecene		(4)					
(Octadecene?)		(4)					
Nonadecene		(4)					
Eicosene		(4)					
Heneicosene		(4)					
Cyclopentadiene			(4)				

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
Cyclopentene		(4)		
1-Methylcyclopentene		(4)	2.8 (6)	0.1-5.0 (6)
			0.4 (7)	0.1-2.4 (7)
3-Methylcyclopentene		(4)		
Cyclohexene				
(2,3-dimethylpentane; 2-methylhexane)[a]	(4)	(4)	9.2 (6)[a]	4.9-43.3 (6)
			62.9 (7)[a]	4.5-48.3 (7)
3-Methylcyclohexene		(4)		
4-Methylcyclohexene		(4)		
(1,7-Octadiyne?)	(4)			
n-Nonane	8.2 (16)		3.1 (6)	0.1-3.8 (6)
			5.5 (16)[a]	
				0.9-10.4 (7)
1-cis-4-Dimethylcyclohexane			2.4 (7)	0.2-3.4 (7)
3-Methyloctane			--	0.6-2.5 (7)
2,6-Dimethyloctane			29.4 (7)	1.6-23.5 (7)
n-Decane	10.9 (16)		2.4 (16)[a]	
n-Undecane	21.4 (16)		4.4 (16)[a]	
n-Dodecane	26.1 (16)		4.5 (16)[a]	
n-Tridecane	24.2 (16)		2.9 (16)[a]	
n-Tetradecane	20.8 (16)		2.4 (16)[a]	
BENZENE AND ALKYL BENZENES				
Benzene (cyclohexane)[a]	2.9-18.7 (2)	17.0 (1)	57.0 (6)[a]	3.6-23.6 (6)
norcyclohexane (7)		0.64-14.7 (2)	153.9 (7)	14.2-288.7 (7)
			113 (17)	22.1 (7)
			190-397 (18)	14-68 (18)
			19.9 (19)	12-158 (18)
Toluene				
(2,3-dimethylhexane)[a]	1.0-4.2 (2)	47.2 (1)	151.4 (6)[a]	17.2-93.5 (6)
		1.4-21.9 (2)	206.7 (7)[a]	14.2-472.9 (7)
	11.4 (16)		206 (17)[b]	34.5 (17)
			35.8 (16)	
		168-578 (18)		
Ethylbenzene				
(2,3-dimethylheptane)[a]		2.8 (1)	10.2 (6)[a]	1.0-7.5 (6)
			48.8 (7)[a]	2.8-31.7 (7)
			39.2 (17)	8.5 (17)
	4.3 (16)		10.9 (16)[b]	
p-Xylene, m-Xylene				
(4-methyloctane)[a]		16.4 (1)	34.2 (6)[a]	2.2-23.3 (6)
			163.2 (7)[a]	10.3-115.9 (7)
o-Xylene				
(unk. C9 paraffin)[a]		4.4 (1)	151.6 (6)[a]	1.3-9.6 (6)
			83.8 (7)[a]	4.5-54.0 (7)
n-Propylbenzene	2.1 (16)	0.8 (1)	1.2 (6)	0.1-1.5 (6)
			12.9 (7)	1.5-9.4 (7)
			3.2 (16)[b]	

Chemical	EMISSION mg/mi Diesel (ref)		Gasoline unspecified (ref)		Gasoline noncatalyzed (ref)		Gasoline catalyzed (ref)	
1-Methyl-3-ethylbenzene (unk. C9 paraffin)[a]			2.5	(1)	7.4	(6)[a]	1.2-5.0	(6)
					77.4	(7)	4.8-55.8	(7)
1-Methyl-2-ethylbenzene (unk. C9 paraffin)[a]					5.4	(6)[a]	0.7-1.9	(6)
							6.3	(7)
n-Pentadecane	17.5	(16)			2.3	(16)[b]		
n-Hexadecane	8.9	(16)			2.1	(16)[b]		
n-Heptadecane	3.9	(16)			1.8	(16)[b]		
Mesitylene			4.3	(1)	3.6	(6)	1.9-3.8	(6)
					36.7	(7)	3.0-30.1	(7)
1,2,4-trimethylbenzene			4.6	(1)	10.0	(7)	1.3-6.1	
					92.3	(7)	4.2-75.1	(7)
sec-Butylbenzene (n-decane)[a]			0.4	(1)	2.0	(6)[a]	0.1-1.9	(6)
					22.2	(7)[a]	1.6-12.7	(7)
Allyltoluene		(4)						
tert-Butylbenzene				(4)				
C_2 alkylcumene		(4)						
Styrene	2.3	(16)			11.3	(16)[a]		
Methyl styrene	0.3	(16)			1.0	(16)[a]		
SUBSTITUTED BENZENES								
Phenol	1.2-1.8	(18[a,b])					0.65-14.7	(18[a,b])
	5.8	(16)			5.3	(16)[b]		
Methoxybenzene		(4)		(4)				
o-Cresol	0.012-0.022	(17)		(4)			0.011-1.8	(18[a,b])
m-Cresol + p-Cresol	0.038-0.052	(17)		(4)			0.008-1.5	(18[a,b])
2,3-Xylenol		(4)		(4)				
2,4-Xylenol		(4)		(4)				
2,5-Xylenol		(4)		(4)				
3,4-Xylenol				(4)				
3,5-Xylenol		(4)		(4)				
2-Methoxyphenol		(4)						
Other phenols		(4)						
Cinnamaldehyde		(4)						
Salicylaldehyde				(4)				
Tolualdehyde (o and p, possibly also m)		(4)		(4)				
4-Methoxybenzoic aldehyde		(4)						
Ethylbenzaldehyde		(4)		(4)				
Dimethylbenzaldehyde		(4)						
Methyltetralins (two isomers)		(4)						
Dimethyltetralins		(4)						
Trimethyltetralin		(4)						
Alkyltetralins (seven additional isomers)		(4)						
Alkylindenes (two isomers)		(4)						
Trimethylindans (four isomers)		(4)						
Acetophenone		(4)		(4)				
Methylacetophenone		(4)						

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
Dienones	(4)			
Indenones	(4)			
Benzaldehyde			6.7 (10)	
Indanones	(4)			
Methoxyindanones	(4)			
Hydroxyindanones	(4)			
Other ketones	(4)			
Hydroxy cyclocarbonyls	(4)			
Nitrophenols	(4)			
Benzonitrile		(4)		
Benzaldehyde	(15)			
ALIPHATIC ALDEHYDES				
Formaldehyde	16-74 (9)		29.6 (10)	
Acrolein	19-76 (9)		5.1 (10)	
Methacrolein		(4)		
n-Butanal	(4)	(4)		
2-Methylpropanal	(4)	(4)		
2-Butenal	(4)	(4)		
2-Methyl-2-butenal		(4)		
n-Pentanal	(4)	(4)		
3-Methylbutanal		(4)		
n-Hexanal	(4)	(4)		
n-Heptanal	(4)			
n-Octanal	(4)			
n-Decanal		(4)		
Acetaldehyde			8.6 (10)	
Propionaldehyde			6.3 (10)	
Butyraldehyde			12.6 (10)	
Crotonaldehyde			6.3 (10)	
Acetone	(15)			
Formaldehyde	(15)			
Acrolein	(16)			
ALKYL NITRITES				
N-DMA (n-nitrosodimethylamine)	$(0.088\text{-}2.73) \times 10^{-3}$ (12)			
N-MOR (n-nitrosomorpholine)	$(0.06\text{-}2.36) \times 10^{-4}$ (12)			
Ethyl nitrite	"23 cpds."			

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
ALIPHATIC KETONES				
2-Butanone		(4)		
3-Buten-2-one		(4)		
(acetoin and methyl allyl ketone?)	(4)			
3-Methyl-2-butanone		(4)		
Methyl isobutyl ketone		(4)		
Methyl sec-butyl ketone		(4)		
3-Methyl-2-pentanone		(4)		
ALIPHATIC - NITRO				
ALIPHATIC ACIDS				
Propanoic acid	(4)			
Butanoic acid	(4)			
2-Butenoic acid	(4)			
Pentanoic acid	(4)			
Benzoic acid	(4)			
Other carboxylic acids	(4)			
ALIPHATIC ALCOHOLS				
sec-Butanol		(4)		
Allyl alcohol		(4)		
2-Buten-1-ol		(4)		
Hexanol	(4)			
Heptanol	(4)			
Octanol	(4)			

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline non-catalyzed (ref)	Gasoline catalyzed (ref)
PAH (includes biphenyl)				
Naphthalene	11.9 (16)		13.8 (16)[b]	
Phenanthrenes	4.2 (3)			
Anthracenes				
Pyrene	1.13 (3)		0.2 (20)	
Fluoranthene	0.91 (3)		0.3 (20)	
Chrysene	0.032 (3)		0.08 (20)	
Cyclopenta[c,d]pyrene	0.0057 (3)			
Benzo[ghi]fluoranthene	0.046 (3)		0.02 (20)	
Benz[a]anthracene	0.17 (3)			
Acenaphthene	(4)			
Benzo[a]pyrene	(3)			
Triphenylene	(13)			
Diphenylbenzene (terphenyl)	(13)			
Benzofluorenes	(13)			
Benzonaphthalenes	(13)			
Dihydrofluoranthenes	(13)			
Dihydropyrenes	(13)			
1-Methylnaphthalene	0.6 (16)		2.9 (16)[b]	
2-Methylnaphthalene	0.5 (16)		5.5 (16)[b]	
PAH - ACIDS				
PAH - KETONES				
Fluorenones	76.0 (3)			
Methylfluorenones	2.1 (3)			
Dimethylfluorenones	0.53 (3)			
Anthrones	8.8 (3)			
Phenanthrones				
Methylanthrones	5.2 (3)			
Methylphenanthrones				
Xanthones	2.0 (3)			
Methylxanthones	0.50 (3)			
Thioxanthones	4.4 (3)			
Methylthioxanthones	1.8 (3)			
Methyl-9-anthrone	(13)			
Benzo[d,h]anthrone	(13)			
1-Naphtho[c,d]pyrone	(13)			
Dimethylanthrones	(3)			
Dimethylphenanthrones	(3)			
Fluoranthones	(3)			
Pyrones	(3)			
Benzanthrones	(3)			

Chemical	EMISSION Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
		mg/mi		
PAH - NITRO				
Nitrofluorenes	0.091	(3)		
Nitroanthracenes	0.15	(3)		
Nitrophenanthrenes				
1-Nitronaphthalene		(5a,b)		
2-Nitrobiphenyl		(5a,b)		
1-Nitro-2-methylnaphthalene		(5a,b)		
2-Nitronaphthalene		(5a,b)		
3-Nitrobiphenyl		(5a,b)		
4-Nitrobiphenyl		(5a,b)		
2-Nitrofluorene		(5a,b)		
9-Nitroanthracene		(5a,b)		
x-Nitro-y-methylfluorene		(5a,b)		
x-Nitro-y-methylfluorene		(5a,b)		
10-Nitro-9-methylanthracene		(5a,b)		
9-Nitro-1-methylanthracene		(5a,b)		
2-Nitrophenanthrene		(5a,b)		
x-Nitro-y-methylanthracene		(5a,b)		
2-Nitroanthracene		(5a,b)		
x-Nitro-y,z-dimethylanthracene		(5a,b)		
x-Nitro-y,z,z'-trimethylanthracene		(5a,b)		
Nitroterphenyl		(5a,b)		
1,5-Dinitronaphthalene		(5a,b)		
1,8-Dinitronaphthalene		(5a,b)		
7-Nitrofluoranthene		(14)		
2,5-Dinitrofluorene		(14)		
2,7-Dinitrofluorene		(14)		
2-Nitrofluoranthene		(14)		
3-Nitrofluoranthene		(14)		
8-Nitrofluoranthene		(14)		
1-Nitrofluoranthene		(14)		
4-Nitropyrene		(14)		
1-Nitropyrene		(14)		
2-Nitropyrene		(14)		
3-Nitro-1-methylpyrene		(14)		
6-Nitro-1-methylpyrene		(14)		
8-Nitro-1-methylpyrene		(14)		
7-Nitrobenz[a]anthracene		(14)		
1-Nitrochrysene		(14)		
6-Nitrocyclopenta[c,d]pyrene		(14)		
2,5-Dinitro-9-fluorenone		(14)		
1,3-Dinitropyrene		(14)		
1,6-Dinitropyrene		(14)		
1,8-Dinitropyrene		(14)		
3-Nitrobenzo[a]pyrene		(14)		
6-Nitrobenzo[a]pyrene		(14)		

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
PAH - ALDEHYDES				
Naphthaldehydes		(4)		
Fluorene carboxaldehydes	8.6	(3)		
Methylfluorene carboxaldehydes	1.2	(3)		
Phenanthrene carboxaldehydes	9.0	(3)		
Anthracene carboxaldehydes				
Methylanthracene carboxaldehydes	3.7	(3)		
Methylphenanthrene carboxaldehydes				
Naphthalene dicarboxaldehydes	3.5	(3)		
Dimethylnaphthalene carboxaldehydes	3.5	(3)		
Trimethylnaphthalene carboxaldehydes	0.0058	(3)		
Pyrene carboxaldehydes	3.1	(3)		
Fluoranthene carboxaldehydes				
Xanthene carboxaldehydes	1.3	(3)		
Dibenzofuran carboxaldehydes	1.1	(3)		
2-Naphthalene carboxaldehydes		(13)		
1-Naphthalene carboxaldehydes		(13)		
Methylnaphthalene carboxaldehydes		(13)		
Naphthalene acetaldehyde		(13)		
Dimethylanthracene carboxaldehydes		(3)		
Dimethylphenanthrene carboxaldehydes		(3)		
Benz[a]anthracene carboxaldehydes		(3)		
Chrysene carboxaldehydes		(3)		
Triphenylene		(3)		
PAH - ALCOHOLS				
Hydroxyfluorene	20.0	(3)		
Methylhydroxyfluorene	1.9	(3)		
Hydroxyanthracenes	3.1	(3)		
Hydroxyphenanthrenes				
Hydroxybiphenyl		(4)		
2-Hydroxybiphenyl		(23 cpds identified)		
Dihydroxyfluorene		(13)		
Dihydroxyanthracene		(13)		
Dihydroxymethylfluorene		(13)		
Trihydroxyfluorene		(13)		
Dihydroxydimethylanthracene		(13)		

Chemical	EMISSION mg/mi Diesel (ref)	Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)
Dimethylhydroxyfluorene	(3)			
Hydroxymethylanthracenes	(3)			
Hydroxymethylphenanthrenes	(3)			
Hydroxydimethylanthracenes	(3)			
Hydroxydimethylphenanthrenes	(3)			
Hydroxyfluorenones	(3)			
Hydroxyxanthone	(3)			
Hydroxyxanthene	(3)			
PAH - ACID ANHYDRIDES				
Naphthalene dicarboxylic acid anhydrides	13. (3)			
Hydroxynaphthalene dicarboxylic acid anhydride	(13)			
Methylnaphthalene dicarboxylic acid anhydride	(3)			
Dimethylnaphthalene dicarboxylic acid anhydride	(3)			
Anthracene dicarboxylic acid anhydride	(3)			
Phenanthrene dicarboxylic acid anhydride	(3)			
PAH - QUINONES				
Fluorene quinones	3.7 (3)			
Methylfluorene quinones	1.7 (3)			
Dimethylfluorene quinones	1.0 (3)			
Anthracene quinones	6.0 (3)			
Phenanthrene quinones	(13)			
Methyl-9,10-anthracene quinone	(13)			
Methyl-9,10-phenanthrene quinone	(13)			
Naphtho[2,3b]furan-4,9-dione	(13)			
Benzo[a]anthracene quinone	(13)			
Chrysene quinone	(13)			
Triphenylene quinone	(13)			
Methylfluorene quinone	(13)			
Methylanthracene quinones	(3)			
Methylphenanthrene quinones	(3)			
Fluoranthene quinones	(3)			
Pyrene quinones	(3)			
Naphtho(1,8-c,d)pyrene-1,3-dione	(3)			
ALKYL - PAH				
1-Methylnaphthalene	0.6 (16)		2.9 (16)[b]	
2-Methylnaphthalene	0.5 (16)		5.5 (16)[b]	
Methylphenanthrenes	1.5 (3)			

Chemical	EMISSION mg/mi Diesel (ref)		Gasoline unspecified (ref)	Gasoline noncatalyzed (ref)	Gasoline catalyzed (ref)	
Methylanthracenes						
Dimethylphenanthrenes	1.9	(3)				
Dimethylanthracenes						
Methylpyrenes	0.33	(3)				
Methylfluoranthenes						
Trimethylphenanthrenes		(13)				
Trimethylanthracenes		(13)				
HETEROCYCLICS						
Trimethylthiophene		(4)				
Dimethylbenzothiophenes (two isomers)		(4)				
Furan		(4)	(4)			
Tetrahydrofuran			(4)			
Methylfuran			(4)			
2-Methyltetrahydrofuran			(4)			
2,2,4,4-Tetramethyltetrahydrofuran			(4)			
Benzofuran		(4)	(4)			
Furfural		(4)				
OTHER						
Ethyl sulfide			(4)			
Methyl disulfide			(4)			
Diethylamine			(4)			
Monomethylamine					0.3	(8)
Dimethylamine					0.1	(8)
Total aliphatic amines					2.2	(8)

[a]Concentration given for unresolved components.

[b]Results from Allegheny Highway Tunnel measured for gasoline-powered vehicles with 50% of the vehicles using catalysts.

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APPENDIX B

APPROACHES TO EVALUATING THE HEALTH EFFECTS OF EXPOSURE TO VAPOR-PHASE ORGANICS FOR PURPOSES OF RISK ASSESSMENT

There are three general types of risk assessment: qualitative, comparative, and quantitative. The purpose of each type and the kinds of data it requires are briefly discussed here.

QUALITATIVE RISK ASSESSMENT

The purpose of a qualitative risk assessment is to determine whether a risk is associated with a particular human activity (say, exposure to a substance), to identify the human-health end point as present or absent, and to judge the severity of the risk. No attempt is made to quantify the risk (measure the incidence or frequency of occurrence) in terms of specific health end points--e.g., lives lost, cancer cases incurred, amount of life-shortening expected, or morbidity projected. Qualitative risk assessments are useful in summarizing the scientific information on a particular kind of exposure. Such assessments could be applied to all 23 compounds in Table 1, more precisely in some cases than in others.

COMPARATIVE RISK ASSESSMENT

The purpose of a comparative risk assessment is to examine the relationship of two or more human activities or exposures to determine their relative risks. For example, in studying exposures to exhaust from diesel vs. gasoline engines, one might attempt to compare the frequency of various health end points. These comparisons could be made: A is riskier than B or A is twice as toxic as B, with respect to a particular end point. Such comparative assessments--based on exposure to vapor-phase organic substances in the exhaust of diesel vs. gasoline engines--for specific end points could be applied to some but probably not all 23 of the substances listed in Table 1. Such could be done for substances listed in Table 2 on which toxicologic data are available. The validity of the comparison in each case would depend on the quality and amount of toxicity data available. Comparative risk assessments are useful mainly in weighing actions that could be taken in policy decisions and in priority-setting for toxicity testing.

Comparative risk assessment based on the genetic impact of various environmental mutagens has been discussed in some detail in a recent NRC report (1982). In that report, comparative risk assessment based on mutagenic testing is referred to as semiquantitative risk estimation. A scheme for comparative risk estimation of carcinogens based on ranking has been proposed recently by Squire (1981).

QUANTITATIVE RISK ASSESSMENT

Quantitative risk assessment involves the estimation of risk associated with a specific exposure of a specific population. For general discussions of quantitative risk, see Cornfield (1977), Food Safety Council (1980), Van Ryzin (1981), Armitage (1982), or Krewski and Van Ryzin (1981). Quantitative risk assessment includes a number of the following steps.

- Health-hazard data identification and data evaluation.
- Dose-response assessment.
- Extrapolation from high doses to low doses.
- Interspecies conversion.
- Population identification.
- Evaluation of uncertainties.

A brief description of the steps mentioned above follows:

DATA IDENTIFICATION AND EVALUATION

The data to be used must be assembled and evaluated. The relevant toxicity and exposure data might include epidemiologic data, animal bioassay data, short-term test data, and mutagenicity data. Typically, the data to be used are from epidemiologic studies or animal bioassays, because these lead to quantification through dose-response estimation, species conversion, or conversion to doses consistent with human exposure. If a variety of such data sets exist, either the best data are used or separate risk estimates are derived from each of the data sets and are later combined to arrive at an overall estimate.

DOSE-RESPONSE ASSESSMENT

Two types of data are used in estimating a dose-response relation from a given set of dose data: quantal data (or counts of responses) and time-to-response data. When quantal data are used, the data are tabulated according to exposure dose, and the number of subjects responding with the end point of interest at each dose is recorded. For example, in an animal bioassay, if the experiment contains four dose groups (control, low, intermediate, and high), animals in each group responding with a specific health end point are counted. The dose-response relation can be discovered with various dose-response models. Detailed information on models can be found in Krewski and Van Ryzin (1981). These estimates of

the dose-response model can be analyzed with statistical estimation procedures (see, for example, Krewski and Van Ryzin, 1981). After a dose-response curve is constructed, the next step is extrapolation to appropriate human exposures. The second type of data that can be used in quantitative risk assessment is time-to-response data (see, for example, Kalbfleisch and Prentice, 1980; Kalbfleisch et al., 1983; or Hartley and Sielken, 1977). Again, the estimates derived are extrapolated to human doses and periods of exposure that are relevant for the population under study.

EXTRAPOLATION FROM HIGH DOSES TO LOW DOSES

Because the exposure doses of interest in most risk assessments tend to be much lower than those in the data base (that is, in the dose-response curve), the high exposures of treated animals must be extrapolated to lower or likely exposure doses. Such extrapolation usually depends heavily on the mathematical model used in estimation (see, for example, Van Ryzin, 1980; Krewski and Van Ryzin, 1981). Thus, the extrapolations or estimates for low doses should be accompanied by confidence-interval estimates and by statements on the uncertainties encountered in the process. Moreover, given proper biologic and statistical input, suitable low-dose estimates of risk or a range of estimates can often be given. However, these estimates of low-dose risk are for the animal species tested, not (usually) for humans, so the next step in risk assessment is interspecies conversion.

INTERSPECIES CONVERSION

The conversion of test-animal exposures to relevant human exposures always constitutes a serious problem when animal bioassay data are used. The method of conversion may depend on the route of exposure in the test species and man, the metabolic pathways involved, the target organ of toxicity, and so on. Such conversion is always judgmental and is a source of uncertainty in any risk assessment based on animal data. Assuming that conversion is possible, the next step in risk assessment is to determine the human population at risk.

POPULATION TO WHICH RISK ESTIMATES ARE APPLIED

In any risk assessment, the population at risk must be determined. The end points of interest must be specified, and the risk estimates for such end points established at various doses likely to be encountered. Patterns of exposure of various subgroups in the population of interest must be ascertained. For example, if one is estimating the risk associated with a chemical in the vapor-phase component of diesel exhaust, one must estimate the exposure of various subpopulations (commuters, drivers, etc.) and then the subpopulations must be combined by some

averaging process to arrive at a risk for an overall population. The latter requires suitable exposure information and knowledge of population characteristics.

EVALUATION OF UNCERTAINTIES IN RISK ESTIMATION

As can be seen from the above discussion, many uncertainties are inherent in any quantitative risk assessment--in the choice of data to use, the choice of mathematical models for extrapolation, the choice of interspecies conversion factor, the estimation of exposure, the combination of estimates based on data of different sources, the combination or weighting of toxic end points considered, and the method of choosing and averaging the subpopulations at risk. All these are somewhat judgmental, so any quantitative risk assessment must be accompanied by scientific justification of the choice made at each step of the process and a statement of the uncertainties that attend the choices. A variety of estimates or a range of estimates of risk, rather than a single number, may well be appropriate. In fact, a full quantitative risk assessment may incorporate a fairly large set of estimates with ranges. For example, in the National Research Council report (1981) on nitrate, nitrite, and nitrosamines, a risk assessment was done for seven different subpopulations of interest.

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APPENDIX C

APPROACH TO EXPOSURE ASSESSMENT

INTRODUCTION

The feasibility study could not review in depth all the approaches to calculating the concentration of chemicals to which humans are exposed, but it is essential to discuss briefly whether there are practical approaches.

Exposure assessment is an integral part of risk assessment. Thus, the concentrations of the chemicals in question must be estimated, with an eye to learning whether exposures are within known or suspected ranges of risk.

ESTIMATING EXPOSURE BY MODELING*

Estimation of potential exposure of a selected population requires quantitative vehicle-emission data and models for determining the atmospheric dispersion of what is emitted. The composition of vehicle emission of all sources appears to be qualitatively similar. However, important quantitative differences are related to type of engine, fuel, engine operating conditions, and temperature.

CALCULATION OF EMISSION RATES

Since 1960, many studies have been undertaken to measure vapor-phase vehicle emission qualitatively and quantitatively. Those studies have generated data on the vapor-phase constituents in several categories:

- Qualitative data.
- Quantitative data expressed in parts per million (volume/volume) of an exhaust sample.
- Quantitative data expressed in milligrams of vapor-phase emission per mile.
- Quantitative data expressed in other units, such as milligrams of vapor-phase emission per unit of fuel used.

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*This is only one of several approaches and is included here to exemplify the state of the art.

Only 16 of the approximately 250 papers published since 1960 contained concentration data on chemicals expressed either directly in milligrams per mile or in some other form suitable for calculating emission rates. These data are summarized in Appendix A.

A number of recent studies have measured the concentrations of compounds adsorbed on diesel-exhaust particles. Three studies (Cautreels and Van Cauwenberghe, 1978; Schuetzle, 1983; Stenberg, 1983) gave data on the partitioning of constituents between the particulate and gas phases (see Table C-1). The Committee found that there is an empirical relationship between the boiling point and the particulate- to gas-phase partition coefficient (P/G) for several of these compounds. There is a linear relationship between molecular weight and boiling point for the polycyclic aromatic hydrocarbons (PAH) compounds and a different linear relationship for the aliphatic hydrocarbons. These data are presented in Figure C-1. The gas-phase emission rates for a number of compounds have been calculated on the basis of this relationship (see Appendix A).

CALCULATION OF DISPERSION (DILUTION) RATES

A tracer or surrogate model can be used to determine the annual mean concentration of a gas-phase component. The model uses CO as the tracer and assumes that, under similar dispersion conditions, the proportionality between the ambient concentration of CO and the emission rates of carbon monoxide and the subject nonreactive airborne chemical species is similar for all chemical species. Several studies have determined the contribution of various sources to the total CO measured in an urban area. One of these efforts took place in conjunction with the Regional Air Pollution Study (RAPS) in St. Louis. The average yearly concentration of CO was found to be y ppm. An emission inventory has been developed for the St. Louis metropolitan area that can be used to estimate the relative contributions of various sources (e.g., vehicles, power plants, and open burning) to the total burden of CO. A percentage of the CO found in the atmosphere can be attributed to all vehicular sources. During the period in question, there were five main categories of on-road vehicular sources: light- duty gasoline vehicles, noncatalyzed (LDG-NC); light-duty gasoline vehicles, catalyzed (LDG-C); heavy-duty gasoline vehicles (HDG); light-duty diesel vehicles (LDD); and heavy-duty diesel vehicles (HDD). From the total miles driven for each vehicle type in St. Louis and their average CO emission rates, the percentage contribution of each vehicle type to ambient-air CO can be calculated. The average annual concentration for a gas-phase component, C(x), in the atmosphere that has been emitted from a particular vehicle category (e.g., LDG-NC) in St. Louis can be calculated with this equation:

$$C(x) = [E(x)/E(CO)][C(CO)],$$

where C(CO) is the average yearly concentration of CO due to emission from a particular vehicle catetory, E(x) is the average emission rate (mg/mile) of component x (see Appendix A), and E(CO) is the average emission rate (mg/mile).

Table C-1

Particulate- and Gas-Phase Partitioning of Some Polycyclic Aromatic Hydrocarbons and Aliphatic Hydrocarbons Used in Figure C-1

Compound	Reference	Boiling Point, C	Particle/Gas Distribution Factor (P/G)	Molecular Weight
Hydrocarbons:				
n-Nonadecane	(2)	330	0.05	268
n-Eicosane	(2)	343	0.11	282
n-Heneicosane	(2)	356	0.26	296
n-Docosane	(2)	369	0.55	310
n-Tricosane	(2)	380	1.41	324
n-Tetracosane	(2)	391	1.76	338
n-Pentacosane	(2)		1.66	352
n-Hexacosane	(2)	412	1.12	366
n-Heptacosane	(2)	422	1.39	380
PAH:				
Phenanthrene and anthracene	(2)	340	0.03	178
	(7)	340	0.20	178
	(8)	340	0.06	178
Fluoranthene	(2)	375	0.26	202
	(7)	375	0.97	202
	(8)	375	0.39	202
Pyrene	(2)	380	0.49	202
	(7)	380	0.75	202
	(8)	380	0.48	202
Benz[a]anthracene and chrysene	(2)	435,438 441 (av.)	3.15	228
	(7)	435,438 441 (av.)	1.23	228
	(8)	435,438 441 (av.)	1.44	228
Benzo[a]pyrene + isomers	(2)		7.47	252
	(7)		21.0	252
	(8)		3.8	252
PAH quinones:				
Anthracene quinone	(2)	380	0.28	208
Phenanthrene quinone	--	360	--	208
PAH-ketone:	--	342	--	180
9-Fluorenone				
Nitro-PAH:				
2-Nitronaphthalene	--	304	--	218

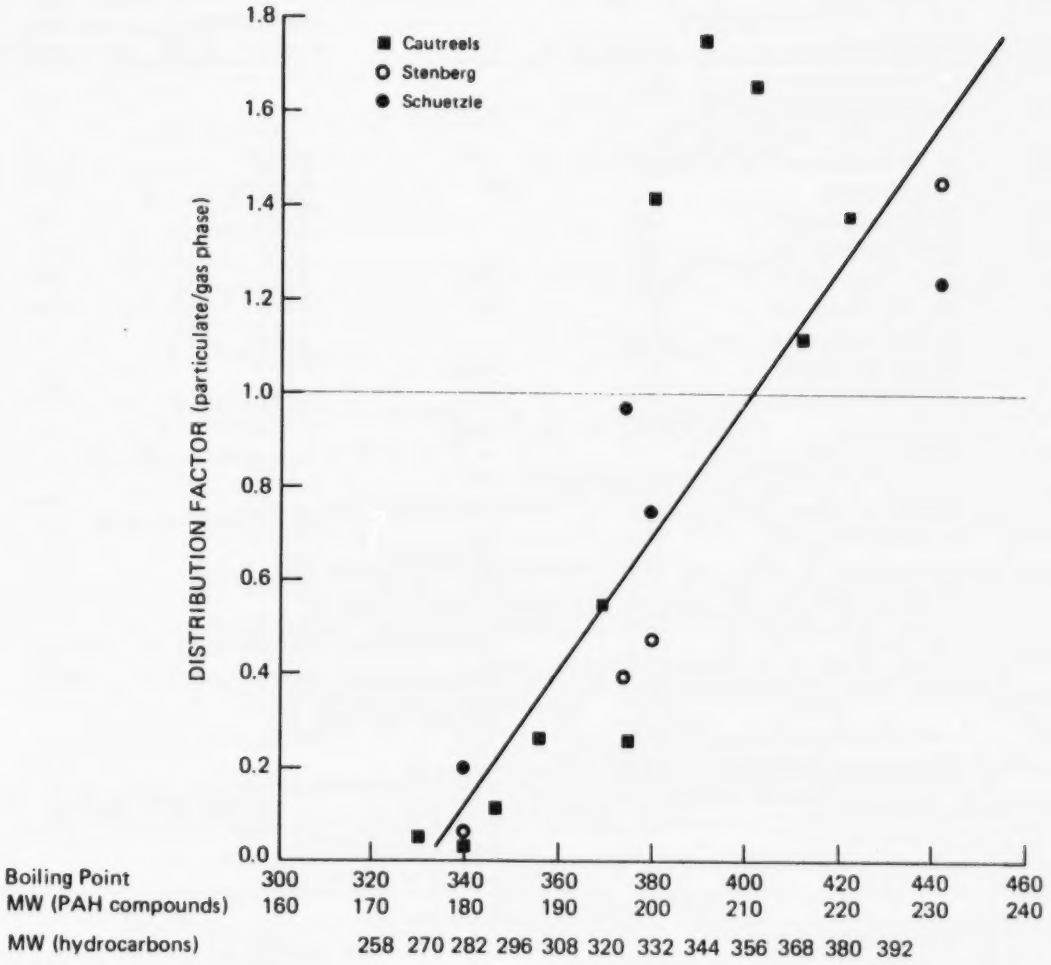

FIGURE C-1. Distribution of compounds in the particulate and gas phases as a function of boiling point and molecular weight.

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